REMARKS

The Examiner rejected claims 9-23 under 35 U.S.C. 112 for the reason suggested in paper 19. Paper 19 rejected claim 9-23 on the basis that the claims are drawn to a method of detecting both full-length receptor and soluble receptor but that require the detection of soluble receptor. In the final office action of July 29, 2003, the Examiner stated that removing the "and full-length epidermal growth factor receptor" in the preamble of claim 9 would overcome the basis of the objection. Accordingly, Applicants have deleted the phrase as suggested by the Examiner and have further removed the word soluble from the preamble and in part d of the claim to make the claim consistent throughout. Applicants believes this amendment puts at least claims 18 through 23 in a condition for allowance as no other objection has been raised to those claims.

Applicant notes that claim 9 is drawn to biological specimen, which would include tissue, and claim 11 is limited to biological fluids in which only soluble epidermal growth factor receptor exists. The above amendment provides that whatever form of epidermal growth factor exists in various fora will be detected. Applicant did not claim that its ALISA could discern full-length from soluble forms, simply that the full-length form was not found in certain biological specimen and thus it was necessarily detecting the soluble form.

The Examiner rejected claims 9-17 "for the reasons of record in the office action of papers nos. 14 and 19." Paper no. 14 stated that the invention was unpatentable over Harvey et al., U.S. patent 6,674,753, 1997, Partanen et al. (J. Occup. Med., 1994, vol. 36 pp 1324-1328) or Witters et al. (Clin. Cancer Res., 1995, vol. 1, pp. 551-557) in view of Graus-Porta et al. or Olayioye et

al., and further in view of WO 94/11734 (Johansen et al., 1994).

The Examiner rejected Applicants' arguments stating that the antibodies were known, the conditions are not claimed, and there is nothing in this assay that are unique to Applicants' invention that are not encountered with all other antibody assays. Applicants' prior comments show that the inventions cited by the Examiner do not teach the present invention, their combination does not result in Applicants' invention, and they do not make Applicants' invention obvious. The Baron paper cited was cited to show that Applicant is aware of the prior art cited by the Examiner and the limitations of that prior art and analysis of that prior art to enable the Examiner to appreciate the differences more concretely and that it would not have been obvious to combine them even if their combination would result in Applicants' invention.

CONCLUSION

Applicants respectfully submit that the present invention is not obviated or anticipated by the teachings and that the patent application and claims therein, as amended, are in a condition for allowance. Reconsideration is, therefore, respectfully requested.

Respectfully submitted,

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Complete Listing of All Claims:

Claim 1 (withdrawn): An isolated nucleic acid selected from the group consisting of:

a) a nucleic acid which encodes a protein comprising the amino acid sequence SEQ ID NO. 1,

b) a nucleic acid which encodes a protein comprising an amino acid sequence which is at least 90% identical to SEQ ID NO. 1 and which has at least 50% of the biological activity of the protein SEQ ID NO. 1,

c) a nucleic acid which is complementary to nucleic acid a) or b).

Claim 2 (withdrawn): The isolated nucleic acid of claim 1 wherein the nucleic acid has the sequence SEQ ID NO. 2.

Claim 3 (withdrawn): The isolated nucleic acid of claim 1 wherein the nucleic acid encodes a protein comprising the amino acid sequence SEQ ID NO. 3.

Claim 4 (withdrawn): The isolated nucleic acid of claim 1 wherein the nucleic acid encodes a protein comprising an amino acid sequence which is at least 99% identical to SEQ ID NO. 1.

Claim 5 (withdrawn): The isolated nucleic acid of claim 4 wherein the encoded protein comprises an amino acid sequence selected from the group consisting of SEQ ID NO. 4, SEQ ID NO. 5, and SEQ ID NO. 6.

Claim 6 (withdrawn): An immunogenic conjugate comprising an immunogenic carrier molecule and a polypeptide of between 10 and 500 amino acids in length comprising an amino acid sequence of 10 to 25 amino acids in length which is identical to an amino acid sequence of the same length contained in an amino acid sequence selected from the group consisting of amino acids 628-705 of SEQ ID NO. 1, amino acids 628-705 of SEQ ID

NO. 4, amino acids 628-705 of SEQ ID NO. 5, and amino acids 628-705 of SEQ ID NO. 6.

Claim 7 (withdrawn): The immunogenic conjugate of claim 6, wherein the polypeptide comprises an amino acid sequence of 11 to 21 amino acids in length which is identical to an amino acid sequence of the same length contained in an amino acid sequence selected from the group consisting of amino acids 628-705 of SEQ ID NO. 1, amino acids 628-705 of SEQ ID NO. 4, amino acids 628-705 of SEQ ID NO. 5, and amino acids 628-705 of SEQ ID NO. 6.

Claim 8 (withdrawn): The immunogenic conjugate of claim 6, wherein the immunogenic carrier molecule is selected from the group consisting of keyhole limpet hemocyanin and bovine serum albumin.

Claim 9 (currently amended): An assay for determining the concentration of ~~soluble~~ epidermal growth factor receptor ~~and full-length epidermal growth factor receptor~~ in a biological sample from a human patient, the assay comprising:

a) obtaining a biological sample from the patient;

b) contacting an amount of a first purified antibody that specifically reacts with a first epitope of the extracellular ligand binding domain of sErbB1 with the patient biological sample to be tested, wherein the first purified antibody is modified with a first labeling moiety;

c) contacting the sample with an amount of a second purified antibody that specifically reacts with a second epitope of the extracellular ligand binding domain of sErbB1, wherein the second purified antibody is modified with a second labeling moiety, and wherein the second purified antibody does not

competitively inhibit the binding of the first purified antibody; and

d) detecting the co-presence of the first and second labels to determine the concentration of the ~~soluble~~ epidermal growth factor receptor complexed with the antibodies; wherein one of the antibodies is chosen from the group consisting of: MAb R.1 and antibodies which competitively inhibit the binding of MAb R.1 to ErbB1; and wherein the other antibody is chosen from the group consisting of MAb 528 and antibodies which competitively inhibit the binding of MAb 528 to ErbB1.

Claim 10 (original): The assay of claim 9 wherein the patient biological sample is chosen from the group consisting of urine and ascites.

Claim 11 (previously amended): The assay of claim 11 wherein the patient biological sample is chosen from the group consisting of blood, serum and plasma.

Claim 12: (original): The assay of claim 11 wherein the first labeling moiety is an affinity binding moiety.

Claim 13 (original): The assay of claim 12 wherein the affinity binding moiety is biotin.

Claim 14 (original): The assay of claim 13 wherein detection of the presence of the first labeling moiety is by binding of the biotin moiety to a solid support coated with a molecule chosen from the group consisting of streptavidin and avidin.

Claim 15 (original): The assay of claim 9 wherein the second labelling moiety is selected from the group consisting of a fluorescent moiety, a colorigenic moiety, and a chemiluminescent moiety.

Claim 16 (original): The assay of claim 9 wherein the second labelling moiety is acridinium.

Claim 17 (original): The assay of claim 16 wherein the detection of the presence of the second labeling moiety is by measuring light emitted from a chemiluminescent reaction utilizing the second labeling moiety.

Claim 18 (original): The assay of claim 9 wherein the patient is female, further comprising the steps of;

e) comparing the concentration of soluble epidermal growth factor receptor obtained in step d) with a normal value; and

f) correlating a decrease in the concentration of soluble epidermal growth factor receptor in the patient biological sample with the presence of an ovarian carcinoma in the patient.

Claim 19 (original): The assay of claim 18 wherein the normal value is obtained by assaying biological samples from females of approximately the same age as the patient.

Claim 20 (original): The assay of claim 18 further comprising the step of performing a second assay on a biological sample obtained from the patient at a point in time after the initial assay.

Claim 21 (original): The assay of claim 20, wherein the patient has undergone treatment for ovarian cancer selected from the group consisting of chemotherapy, radiation therapy, and surgical treatment in the interval between the initial and second assay.

Claim 22 (original): The assay of claim 20, further comprising the step of correlating an increase in the concentration of soluble epidermal growth factor receptor in the patient biological sample with an improved prognosis in the ovarian cancer condition.

Claim 23 (original): The assay of claim 20, further comprising the step of correlating a decrease in the concentration of soluble epidermal growth factor receptor in the patient biological sample with an declining prognosis in the ovarian cancer condition.